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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/710,419	11/09/2000	John M. Tomich	30917	5692

23589 7590 02/25/2003

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	**PAPER NUMBER**
1646	11

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/710,419	TOMICH ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-36 and 42-48* is/are pending in the application.

4a) Of the above claim(s) *18-29 and 42-47* is/are withdrawn from consideration.

5)☒ Claim(s) *48* is/are allowed.

6)☒ Claim(s) *30-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison B* .

DETAILED ACTION

Formal Matters

Newly presented, in Paper No. 11, 12/3/2002, claim 42 has been renumbered as claim 48 pursuant to 37 CFR 1.128. Claim 41 was cancelled, and new claim 48 was added in Paper No. 11, 12/3/2002. Claims 18-36, 42-48 are pending. Claims 18-29, 42-47 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 30-36, 48 are under consideration.

Interview

The interview with Tracey Truitt is acknowledged. Due to an error, the sequence of SEQ ID NO: 1 was searched. The Examiner regrets the inconvenience. The species of SEQ ID NO: 18 is under consideration.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of altering the flux of water across a membrane with a peptide of SEQ ID NO: 18, does not reasonably provide enablement for a method of altering the flux of water across a membrane with a variant peptide of SEQ ID NO: 18 having at least about 35%, 50%, or 65% amino acid sequence homology to SEQ ID NO: 18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 30-36 are overly broad in the recitation of "having at least about 35%, 50%, or 65% amino acid sequence homology to SEQ ID NO: 18" since insufficient guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of altering water flux across a membrane. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is insufficient guidance provided in the specification as to how one of ordinary skill in the art would practice a method of altering the flux of water across a membrane with a variant peptide of SEQ ID NO: 18 having at least about 35%, 50%, or 65% amino acid sequence homology to SEQ ID NO: 18. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of

experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 30-36 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Applicant argues that the specification provides examples of peptides with less than 35% sequence homology that retain the function of altering water flux across a cell membrane. Applicant further argues that 52 variations of the M2GlyR sequence have been presented. However, as noted in the response (see Paper No. 10, 12/3/2002 at 4), the sequences are highly divergent, and share little sequence homology. Thus, the specification does not disclose the critical residues necessary to maintain function and does not disclose the correlation between the structure (sequence) of the polypeptides and the function of altering water flux across a membrane. The amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the peptides are lacking, it is unpredictable as to which peptide variations, if any, meet the limitations of the claims. In the instant case there are a large number of peptide species that are 35% identical to SEQ ID NO: 18. SEQ ID NO: 18 is 27 amino acids in length, and at 35% homology up to about 9 amino acids could be substituted with any one of the 19 other amino acid residues. This encompasses a large number of potential peptide sequences, and since the specification does not disclose the

correlation between the sequence of the peptide and the function of altering water flux, it would require undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

Claims 30-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claim. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 18 Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art

do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 18 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant argues that the structural limitations and teachings in the specification of mutations of the peptides which function to alter water flux across a membrane sufficiently describe the genus. Applicant further argues that 52 variations of the M2GlyR sequence have been presented. However, as noted in the response (see Paper No. 10, 12/3/2002 at 4), the sequences are highly divergent, and share little sequence homology. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, there are a large number of peptide species that are 35% identical to SEQ ID NO: 18. SEQ ID NO: 18 is 27 amino acids in length, and at 35% homology up to about 9 amino acids could be substituted with any one of the 19 other amino acid residues. This encompasses a large number of potential peptide sequences and there is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which

variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed: there is no guidance in the art as to what the defining characteristics of the peptides might be. Thus, no identifying characteristics or properties of the instant polynucleotides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, the disclosure of SEQ ID NO: 18 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in claim 33 is a relative term which renders the claim indefinite. The term " substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-36 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9726905 (Iwamoto et al.).

Iwamoto et al. discloses peptides which can alter the flux of water across a membrane. The peptide disclosed in Iwamoto is 65.5% identical to the peptide of SEQ ID NO: 18 of the instant application (see Sequence Comparison B, attached.). The peptides are water soluble to at least 10 mM and enables anions to be transported through a membrane of an epithelial cell when they are embedded in the membrane (page 6, lines 10-19). The peptides exhibit at least 50% helical content (page 6, lines 10-19). The channel assembly can be used to alter the flux of water across an epithelial cell, particularly for treatment of cystic fibrosis (where affected cells are in the airway, pancreatic duct or epididymis). Iwamoto discloses methods of using the peptides to alter the flux of water across a membrane (page 14, lines 5-34) thus claims 30-36 are anticipated.

Conclusion

Claims 30 –36 are rejected.

Claim 48 is allowable.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
February 20, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

SEQIDNO:18

RESULT 1
AAW22819
ID AAW22819 standard; peptide; 27 AA.
XX
AC AAW22819;
XX
DT 13-MAR-1998 (first entry)
XX
DE M2GlyR based channel-forming peptide 17.
XX
KW Channel-forming peptide; channel assembly; epithelial cell; treatment;
KW cystic fibrosis; polycystic kidney disease; anion transportation; M2GlyR.
XX
OS Synthetic.
OS Homo sapiens.
XX
PN WO9726905-A1.
XX
PD 31-JUL-1997.
XX
PF 27-JAN-1997; 97WO-US01103.
XX
PR 24-JAN-1997; 97US-0789155.
PR 25-JAN-1996; 96US-0591381.
PR 23-JAN-1997; 97US-0591381.
XX
PA (UNIV) UNIV KANSAS MEDICAL CENT.
PA (UNIV) UNIV KANSAS STATE RES FOUND.
XX
PI Iwamoto T, Sullivan LP, Tomich JM;
XX
DR WPI; 1997-393366/36.
XX
PT Channel assembly for transporting ions across epithelial cell
PT membranes - comprises new water soluble peptide(s), for treating
PT cystic fibrosis and polycystic kidney disease by altering water flux
PT across cells
XX
PS Claim 16; Page 58; 93pp; English.
XX
CC This peptide is a modified M2GlyR peptide (AAW22803) with additional
CC lysine residues at the N-terminal. This channel-forming lysine analog
CC of the M2GlyR peptide is used to construct a novel channel assembly,
CC comprising 3-6 novel peptides, of 18-30 amino acids. Suitable protein
CC fragments for use as such peptides are present in the strychnine-binding
CC alpha-subunit of the inhibitory glycine receptor (M2GlyR) from human
CC brain, the inhibitory gaama-aminobutryic acid receptor from human brain,
CC and the cystic fibrosis transmembrane conductance regulator from human
CC epithelium. The peptides are synthesized by standard solid phase peptide
CC synthesis. The peptides are water soluble to at least 10 mM and enables
CC anions to be transported through a membrane of an epithelial cell when
CC they are embedded in the membrane. The channel assembly can be used to
CC alter the flux of water across an epithelial cell, particularly for
CC treatment of cystic fibrosis (where affected cells are in the airway,
CC pancreatic duct or epididymis). The channel assembly can also be used in
CC the treatment of autosomal dominant polycystic kidney disease (where the
CC affected cells are in the cystic epithelium). The channel assembly
CC spontaneously inserts into the basolateral membrane to prevent water
CC flow to adjacent cysts.
XX
SQ Sequence 27 AA;

  Query Match   65.5%; Score 86.5; DB 18; Length 27;
  Best Local Similarity   77.8%; Pred. No. 2.4e-06;
  Matches   21; Conservative   1; Mismatches   4; Indels   1; Gaps   1;

Qy   1 KKKKPARVGLGITTVL-VTTIGLGVRA 26
           ||||||||||||||| :|| | ||

Db 1 KKKKPARVGLGITTVLTMTTQSSGSRA 27

RESULT 1
US-09-093-227-17
; Sequence 17, Application US/09093227
; Patent No. 6077826
; GENERAL INFORMATION:
; APPLICANT: Tomich, John M.
; APPLICANT: Iwamoto, Takeo
; APPLICANT: Sullivan, Lawrence P.
; TITLE OF INVENTION: A Synthetic Macromolecular Channel
; TITLE OF INVENTION: Assembly for Transport of Chloride Ions through Epithelium
; TITLE OF INVENTION: Useful in Treating Cystic Fibrosis
; NUMBER OF SEQUENCES: 31
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Hovey, Williams, Timmons & Collins
; STREET: 2405 Grand Blvd., Ste. 400
; CITY: Kansas City
; STATE: Missouri
; COUNTRY: USA
; ZIP: 64108
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/09/093,227
; FILING DATE:
; CLASSIFICATION:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 08/789,155
; FILING DATE: January 24, 1997
; CLASSIFICATION:
; ATTORNEY/AGENT INFORMATION:
; NAME: Collins, John M.
; REGISTRATION NUMBER: 26,262
; REFERENCE/DOCKET NUMBER: 23867B
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (816) 474-9050
; TELEFAX: (816) 474-9057
; INFORMATION FOR SEQ ID NO: 17:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 27 amino acids
; TYPE: amino acid
; STRANDEDNESS:
; TOPOLOGY: linear
; MOLECULE TYPE: peptide
; HYPOTHETICAL: NO
; FRAGMENT TYPE: internal
; ORIGINAL SOURCE:
; TISSUE TYPE: Brain
US-09-093-227-17

Query Match 65.5%; Score 86.5; DB 3; Length 27;
Best Local Similarity 77.8%; Pred. No. 7.3e-07;
Matches 21; Conservative 1; Mismatches 4; Indels 1; Gaps 1;

Qy 1 KKKKPARVGLGITTVL-VTTIGLGVRA 26
||||||||||||||| :|| | ||
Db 1 KKKKPARVGLGITTVLTMTTQSSGSRA 27

RESULT 1
T18791

gamma-aminobutyric acid/benzodiazepine receptor gamma-2 chain precursor - Caenorhabditis elegans
C;Species: Caenorhabditis elegans
C;Date: 15-Oct-1999 #sequence_revision 15-Oct-1999 #text_change 29-Oct-1999
C;Accession: T18791; T27617
R;McMurray, A.
submitted to the EMBL Data Library, March 1997
A;Reference number: Z19022
A;Accession: T18791
A;Status: preliminary; translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-499 <WIL>
A;Cross-references: EMBL:Z93372; PIDN:CAB07549.1; GSPDB:GN00021; CESP:ZC482.5
A;Experimental source: clone BE10
R;McMurray, A.
submitted to the EMBL Data Library, March 1997
A;Reference number: Z20393
A;Accession: T27617
A;Status: preliminary; translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-499 <WI2>
A;Cross-references: EMBL:Z93397; PIDN:CAB07722.1; GSPDB:GN00021; CESP:ZC482.5
A;Experimental source: clone ZC482
C;Genetics:
A;Gene: CESP:ZC482.5
A;Map position: 3
A;Introns: 28/2; 65/1; 88/3; 165/2; 241/1; 323/2; 362/3; 452/3
C;Superfamily: acetylcholine receptor

  Query Match 52.7%; Score 69.5; DB 2; Length 499;
  Best Local Similarity 61.5%; Pred. No. 0.041;
  Matches 16; Conservative 4; Mismatches 5; Indels 1; Gaps 1;

```
Qy      1 KKKKPARVGLGITTVL-VTTIGLGVR 25
          |:  |||| ||| ||| ::||| |:|
Db    281 KEASPARVSLGIMTVLSMSTIGFGLR 306
```

RESULT 2
A49970
glycine receptor alpha-4 chain - mouse (fragment)
C;Species: Mus musculus (house mouse)
C;Date: 17-Nov-1995 #sequence_revision 17-Nov-1995 #text_change 20-Aug-1999
C;Accession: A49970
R;Matzenbach, B.; Maulet, Y.; Sefton, L.; Courtier, B.; Avner, P.; Guenet, J.L.; Betz, H.
J. Biol. Chem. 269, 2607-2612, 1994
A;Title: Structural analysis of mouse glycine receptor alpha subunit genes.
Identification and chromosomal localization of a novel variant alpha4.
A;Reference number: A49970; MUID:94132024; PMID:7507926
A;Accession: A49970
A;Status: preliminary; nucleic acid sequence not shown
A;Molecule type: DNA
A;Residues: 1-337 <MAT>
A;Cross-references: GB:X75850; NID:g435513; PIDN:CAA53468.1; PID:g817957
C;Genetics:
A;Gene: Gla4
C;Superfamily: acetylcholine receptor
C;Keywords: neurotransmitter receptor; transmembrane protein

  Query Match 50.4%; Score 66.5; DB 2; Length 337;
  Best Local Similarity 73.9%; Pred. No. 0.074;
  Matches 17; Conservative 1; Mismatches 4; Indels 1; Gaps 1;

```
Qy      5 PARVGLGITTVL-VTTIGLGVRA 26
          ||||||||||| :||   | ||
Db    261 PARVGLGITTVLTMTTQSSGSRA 283
```

```
RESULT 1
O17555
ID   O17555      PRELIMINARY;      PRT;   499 AA.
AC   O17555; O18279;
DT   01-JAN-1998 (TrEMBLrel. 05, Created)
DT   01-NOV-1998 (TrEMBLrel. 08, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   ZC482.5 protein.
GN   ZC482.5.
OS   Caenorhabditis elegans.
OC   Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditoidea;
OC   Rhabditidae; Peloderinae; Caenorhabditis.
OX   NCBI_TaxID=6239;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Mcmurray A.;
RL   Submitted (MAR-1997) to the EMBL/GenBank/DDBJ databases.
RN   [2]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=94150718; PubMed=7906398;
RA   Wilson R., Ainscough R., Anderson K., Baynes C., Berks M.,
RA   Bonfield J., Burton J., Connell M., Copsey T., Cooper J., Coulson A.,
RA   Craxton M., Dear S., Du Z., Durbin R., Favello A., Fulton L.,
RA   Gardner A., Green P., Hawkins T., Hillier L., Jier M., Johnston L.,
RA   Jones M., Kershaw J., Kirsten J., Laister N., Latreille P.,
RA   Lightning J., Lloyd C., Mcmurray A., Mortimore B., O'Callaghan M.,
RA   Parsons J., Percy C., Rifken L., Roopra A., Saunders D., Shownkeen R.,
RA   Smaldon N., Smith A., Sonnhammer E., Staden R., Sulston J.,
RA   Thierry-Mieg J., Thomas K., Vaudin M., Vaughan K., Waterston R.,
RA   Watson A., Weinstock L., Wilkinson-Sproat J., Wohldman P.;
RT   "2.2 Mb of contiguous nucleotide sequence from chromosome III of C.
RT   elegans.";
RL   Nature 368:32-38(1994).
CC   -!- SUBCELLULAR LOCATION: INTEGRAL MEMBRANE PROTEIN (BY SIMILARITY).
CC   -!- SIMILARITY: BELONGS TO THE LIGAND-GATED IONIC CHANNELS FAMILY.
DR   EMBL; Z93397; CAB07722.1; -.
DR   EMBL; Z93372; CAB07722.1; JOINED.
DR   EMBL; Z93372; CAB07549.1; -.
DR   EMBL; Z93397; CAB07549.1; JOINED.
DR   InterPro; IPR000188; GABAA_receptor.
DR   InterPro; IPR001175; Neur_channel.
DR   Pfam; PF02931; Neur_chan_LBD; 1.
DR   Pfam; PF02932; Neur_chan_memb; 1.
DR   PRINTS; PR00252; NRIONCHANNEL.
DR   TIGRFAMs; TIGR00860; LIC; 1.
DR   PROSITE; PS00236; NEUROTR_ION_CHANNEL; 1.
KW   Glycoprotein; Ionic channel; Postsynaptic membrane; Transmembrane.
SQ   SEQUENCE   499 AA;  57552 MW;  5444AB5AE4AAE256 CRC64;

  Query Match             52.7%;  Score 69.5;  DB 5;  Length 499;
  Best Local Similarity   61.5%;  Pred. No. 0.08;
  Matches   16;  Conservative    4;  Mismatches    5;  Indels    1;  Gaps    1;

Qy       1 KKKKPARVGLGITTVL-VTTIGLGVR 25
             |:  |||| ||| ||| ::||| |:|
Db     281 KEASPARVSLGIMTVLSMSTIGFGLR 306
```

Sequence Comparison B

```
RESULT 1
AAW22819
ID   AAW22819 standard; peptide; 27 AA.
XX
AC   AAW22819;
XX
DT   13-MAR-1998  (first entry)
XX
DE   M2GlyR based channel-forming peptide 17.
XX
KW   Channel-forming peptide; channel assembly; epithelial cell; treatment;
KW   cystic fibrosis; polycystic kidney disease; anion transportation; M2GlyR.
XX
OS   Synthetic.
OS   Homo sapiens.
XX
PN   WO9726905-A1.
PD   31-JUL-1997.
XX
PF   27-JAN-1997;   97WO-US01103.
XX
PR   24-JAN-1997;   97US-0789155.
PR   25-JAN-1996;   96US-0591381.
PR   23-JAN-1997;   97US-0591381.
XX
PA   (UNIV ) UNIV KANSAS MEDICAL CENT.
PA   (UNIV ) UNIV KANSAS STATE RES FOUND.
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PI   Iwamoto T,  Sullivan LP,  Tomich JM;
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DR   WPI; 1997-393366/36.
XX
PT   Channel assembly for transporting ions across epithelial cell
PT   membranes - comprises new water soluble peptide(s), for treating
PT   cystic fibrosis and polycystic kidney disease by altering water flux
PT   across cells
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PS   Claim 16; Page 58; 93pp; English.
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CC   This peptide is a modified M2GlyR peptide (AAW22803) with additional
CC   lysine residues at the N-terminal. This channel-forming lysine analog
CC   of the M2GlyR peptide is used to construct a novel channel assembly,
CC   comprising 3-6 novel peptides, of 18-30 amino acids. Suitable protein
CC   fragments for use as such peptides are present in the strychnine-binding
CC   alpha-subunit of the inhibitory glycine receptor (M2GlyR) from human
CC   brain, the inhibitory gaama-aminobutryic acid receptor from human brain,
CC   and the cystic fibrosis transmembrane conductance regulator from human
CC   epithelium. The peptides are synthesized by standard solid phase peptide
CC   synthesis. The peptides are water soluble to at least 10 mM and enables
CC   anions to be transported through a membrane of an epithelial cell when
CC   they are embedded in the membrane. The channel assembly can be used to
CC   alter the flux of water across an epithelial cell, particularly for
CC   treatment of cystic fibrosis (where affected cells are in the airway,
CC   pancreatic duct or epididymis). The channel assembly can also be used in
CC   the treatment of autosomal dominant polycystic kidney disease (where the
CC   affected cells are in the cystic epithelium). The channel assembly
CC   spontaneously inserts into the basolateral membrane to prevent water
CC   flow to adjacent cysts.
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SQ   Sequence   27 AA;

  Query Match             65.5%;  Score 86.5;  DB 18;  Length 27;
  Best Local Similarity   77.8%;  Pred. No. 2.4e-06;
  Matches   21;  Conservative    1;  Mismatches    4;  Indels    1;  Gaps    1;

Qy       1 KKKKPARVGLGITTVL-VTTIGLGVRA 26
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Db       1 KKKKPARVGLGITTVLTMTTQSSGSRA 27
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